I. AMENDMENTS

AMENDMENTS TO THE CLAIMS

Cancel claim 7 without prejudice to renewal.

1. (Previously presented) A gene-targeted mouse comprising a modified endogenous apolipoprotein E (apoE) allele, wherein said modified allele comprises an apoE-encoding nucleic acid under transcriptional control of endogenous regulatory sequences, wherein the modified allele encodes a modified apoE polypeptide that exhibits domain interaction characteristic of human apolipoprotein E4 (apoE4), wherein the modified apoE polypeptide comprises a Thr → Arg substitution at a position equivalent to amino acid 61 of human apoE4, wherein the gene-targeted mouse is homozygous for the modified apoE allele, and wherein the modified apoE polypeptide exhibits preferential binding to lower density lipoproteins, and wherein the mouse exhibits apoE4-related neurodegeneration.

2.-4. (Canceled)

5. (Previously presented) A cell isolated from the gene-targeted mouse of claim 1, wherein said cell produces the modified apoE polypeptide.

6.-13. (Canceled)

14. (Previously presented) A method of identifying an agent that reduces apoE4-related neurodegeneration, the method comprising:

a) contacting the gene-targeted mouse of claim 1 with a test agent; and

b) determining the effect of the test agent on reducing apoE4-related neurodegeneration.

15.-19. (Canceled)

20. (Previously presented) The cell according to claim 5, wherein said cell is an astrocyte.

21. (Previously presented) The cell according to claim 5, wherein said cell is a microglial cell.

22. (Previously presented) The cell according to claim 5, wherein the cell is a neuronal cell.

23. (Canceled)